REMARKS

Reissue Formalities

The Examiner has objected to the application as lacking the proper written consent of the assignee, and lacking a proper declaration that recites the errors being corrected in the reissue application arose without any deceptive intention on the part of the applicant. Transmitted herewith is a substituted Assent by Assignee, consenting to the filing of the reissue application, as well as a substitute Declaration by the Inventors stating that all errors which are being corrected in the reissue application up to the time of filing of the oath/declaration arose without any deceptive intention on the part of the applicant. The substitute Assent by Assignee and the substitute Declaration by the Inventors are believed to fully comply with the requirements of 37 CFR 1.172(a) and 37 CFR 1.175, and applicants respectfully request the withdrawal of the objection to the executed documents.

Allowable Subject Matter

Applicants acknowledge the Examiner's determination that current claims 11-40 and 58 will be allowed after conformance with the Reissue formalities addressed in the immediately preceding paragraph. The submission of substitute Assent by Assignee and the substitute Declaration by the Inventors are believed to fully address the Examiner's objection and accordingly, claims 11-40 and 58 are believed to be in condition for allowance.

Claim 57 is objected to as being based on a rejected claim. Applicants have amended claim 54 to incorporate the limitations of claim 57, and original claim 57 has been cancelled. The amendment is believed to place claims 54-56 in condition for allowance.

Rejections under 35 USC § 112, second paragraph

Claim 9 stands rejected under 35 USC § 112, second paragraph as being indefinite for the failure of the claim from which it depends (i.e. claim 1) to clearly indicate that a first and second ligand analog component are required. Claim 9 has been amended to place the claim in independent form and to specify that at least a first and second redox reversible species are provided wherein the first and second redox reversible species comprise a liquid sample diffusible conjugate of a ligand analog of an analyte and a redox reversible label. The amendment to the claim is believed to fully address the Examiner's objection under 35 USC § 112, second paragraph, and the claim, now in independent form, is believed to be in condition for allowance.

Claim 41 stands rejected under 35 USC § 112, second paragraph for lack of antecedent basis for the element "said species means". Claim 41 has been amended to replace the objected terminology with the phrase "said diffusible redox reversible species". The amendment is believed to fully address the Examiner's objection and withdrawal of the rejection based on 35 USC § 112, second paragraph is respectfully requested.

Accordingly, applicants respectfully request the withdrawal of the rejection of claims 9, 10 and 41-47 under 35 USC § 112, second paragraph for indefiniteness.

Rejections under 35 USC § 103

Claims 1, 3-5, 41-44, 46-48, 50-52, 54-56 and 59 stand rejected under 35 USC § 103 as being unpatentable over Roberts et al (US Patent 5,958,791). Claims 48-52 have been cancelled rendering the rejection as to those claims moot. Claim 54 has been amended to incorporate the

limitation of original claim 57, rendering the rejection of claims 54-56 moot. With regards to the rejection of claims 1, 3-5, 41-44, 46-47 and 59 applicants respectfully traverse the rejection.

The cited Roberts reference discloses a test device and method for the electrochemical detection of an analyte in a test solution. The device comprises a solid phase "electrochemical measurement portion" comprising a first and second electrical conductor, and a liposome lysing reagent. An analyte binding material, bound to a solid phase, is provided either as part of the electrochemical measurement portion (see Figs. 1 and 5a), or as a separate material that is first incubated with the sample prior to introduction of the sample to the device (see Figs. 3 and 5b). The Roberts disclosed method comprises adding a liposome conjugate to the test solution containing the analyte (optionally in the presence of the analyte binding agent) and contacting the mixture with the device, wherein the liposome conjugate comprises an analyte analog linked to a liposome. The liposome conjugate further comprises an electroactive marker entrapped within the liposome, such that upon contact of the conjugate with the bound liposome lysing agent, the lysosome will release the liposome contents causing an increase in current across the first and second electrodes. The amount of detected current generated is correlated with the amount of analyte present in the sample.

In summary, the Roberts' disclosed method uses conjugates wherein the electroactive marker is indirectly linked to the analyte analog by being entrapped in a liposome. This does not constitute a covalent binding of a redox reversible species as required by the amended claims submitted herein and as defined by applicants at column 10, lines 11-15. Furthermore, the Roberts' method requires the analyte "binding material" to be bound to a solid phase to allow separation between the liposome conjugates that are bound to the analyte binding agent and those liposome conjugates not bound to the analyte binding agent.

Unlike the Roberts' device and methods, applicants provide conjugates wherein the redox reversible species is covalently bound to the ligand analogs of the analyte of interest. In this manner separation between the bound (electroactively blocked) and free (electroactively detectable) ligands is not required. Thus applicants' method can be conducted as a homogenous, separation-free measurement. Roberts on the other hand requires the use of a solid support and separation of the bound and unbound liposome conjugates.

To further clarify the differences between the Roberts invention and the presently claimed invention, independent claims 1, 41 and 59 have been amended to specify that the redox reversible species comprises a liquid sample diffusible covalent conjugate of a ligand analog of said analyte and a redox reversible label. Support for the amendment is found at column 1, lines 63-65 of the application/issued patent. As disclosed at column 10, lines 11-15, a covalent conjugate is intended to encompass conjugates prepared by linking the ligand analog to the label (i.e. the redox reversible label) either covalently through bifunctional linking agents or by combination of covalent linkages and art-recognized specific binding entities (for example, biotin-avidin).

The teaching of Roberts is limited to a non-homogeneous assay wherein the reactants must be separated before measurements are taken. Roberts fails to teach or suggest a homogeneous assay or how to covalently link a redox reversible label to the analyte analog while still retaining the analyte analog's ability to effectively compete with the analyte for binding to the analyte ligand. The procedure described by Roberts simply would not work with a covalently bound conjugate and the binding partners described in the present invention because the conjugates bound to the analyte, and thus retained on the solid support of the Roberts system, are electroactively blocked.

Accordingly, Roberts fails to teach or suggest a method of detecting and quantitating an analyte in a sample through the use of a liquid sample diffusible covalent conjugate of a ligand analog of said analyte in a homogeneous separation-free assay. Therefore, applicants respectfully submit that claims 1, 41 and 58, and all claims depending therefrom, are patentable over the teachings of the Roberts reference. Withdrawal of the rejection of claims 1, 3-5, 41-44, 46-47, 54-56 and 59 is respectfully requested.

Claims 2, 6, 49 and 53 stand rejected under 35 USC § 103 as being unpatentable over Roberts et al (US Patent 5,958,791) in further view of Niwa et al. Applicants note that claim 53 has been cancelled rendering the rejection of that claim moot. Claims 2 and 6, and 49 depend from claims 1 and 41, respectfully. The reasons for the patentability of base claims 1 and 41 over the teachings of Roberts has been discussed in the immediately preceding paragraphs. The secondary Niwa reference fails to provide any additional teachings to supplement the inadequacies of the Roberts reference with regards to the use of a liquid sample diffusible covalent conjugate of a ligand analog of an analyte in a homogeneous separation-free assay, wherein the conjugate comprises the ligand analog covalently bound to a redox reversible label. Accordingly, claims 2, 6 and 49 are believe to be patentable over the combination of Roberts and Niwa for the same reasons that claims 1 and 41 are patentable over the teachings of Roberts alone.

Claims 7 and 8 stand rejected under 35 USC § 103 as being unpatentable over Roberts et al (US Patent 5,958,791) in further view of Spring et al (US Patent 5,643,721). The inadequacies of the Roberts teachings with regards to the invention of claims 1 and 41 have been previously discussed. The secondary Spring et al reference fails to provide any additional teachings to supplement the inadequacies of the Roberts reference with regards to the use of a liquid sample

diffusible covalent conjugate of a ligand analog of an analyte in a homogeneous separation-free assay, wherein the conjugate comprises the ligand analog covalently bound to a redox reversible label. Accordingly, claims 7 and 8 are believe to be patentable over the combination of Roberts and Spring et al for the same reasons that claims 1 and 41 are patentable over the teachings of Roberts alone.

Claim 45 stands rejected under 35 USC § 103 as being unpatentable over Roberts et al (US Patent 5,958,791) in further view of Deng et al (US Patent 5,589,326). The inadequacies of the Roberts teachings with regards to the invention of claims 1 and 41 have been previously discussed. The secondary Deng reference fails to provide any additional teachings to supplement the inadequacies of the Roberts reference with regards to the use of a liquid sample diffusible covalent conjugate of a ligand analog of an analyte in a homogeneous separation-free assay, wherein the conjugate comprises the ligand analog covalently bound to a redox reversible label. Accordingly claim 45 is believe to be patentable over the combination of Roberts and Deng et al for the same reasons that claims 1 and 41 are patentable over the teachings of Roberts alone.

Applicants believe that the present application is now in condition for allowance and such action is respectfully requested. If the Examiner has any questions or comments such that a conversation would speed prosecution of this application, the Examiner is invited to call the undersigned at (434) 220-2866.

Respectfully submitted,

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